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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Karen M. Downs
Serial No.:	09/336,103
Filed:	June 18, 1999
For:	CHIMERIC MAMMALIAN ALLANTOIS
Group Art Unit:	1633
Examiner:	M. Wilson

Commissioner For Patents
Washington, D.C. 20231

DECLARATION OF KAREN M. DOWNS

Dear Sir:

I, Karen M. Downs, declare that:

1. I am the inventor of the above-identified patent application and the first-named author in Downs and Gardner, 1995, cited by the Examiner. I am an Associate Professor in the Department of Anatomy at the University of Wisconsin-Madison.

2. I have read the September 12, 2001 Office Action and wish to disagree with the Examiner's assertion that:

"Attachment of the allantois to the chorion is part of vasculogenesis because attachment of the allantois to the chorion is required for the allantois to become

vascularized (p. 407, column 2, 5 lines from the bottom) and become the umbilical cord."

3. The Examiner's understanding of my statement is not correct. What we have said is that "once chorio-allantoic fusion has begun, the allantois soon becomes overtly vascularized." What we meant by this statement is that blood vessels running down the length of the allantois were recognizable after fusion took place. This statement does not address when allantoic vasculogenesis began and whether the chorion was required for allantoic vascularization.

4. In fact, we demonstrated that fusion with the chorion is not required for allantoic vascularization in the following papers:

Downs and Gardner, 1995, Fig. 4B, D p. 411. Example of an allantois regenerate that has not fused with the chorion contains a nascent blood vessel. At later developmental timepoints (Fig. 4D), such allantoic blood vessels contained red blood cells.

This observation is further discussed on p. 415, column 2, first paragraph: "Hence, this confirms that contact with the chorion is not required to initiate vascularization of the allantois.

Downs and Harmann, 1997, p. 2779, column 2, last paragraph: "Allantoic vascularization is not dependent

upon fusion with the chorion . . . . We have found that angioblasts are formed almost as soon as the allantois emerges from the posterior primitive streak.

Downs, et al., 1998, p. 4517, second column, "Distal-to-proximal sequence of allantoic vasculogenesis: The observed spatiotemporal sequence in morphological and molecular differentiation in the allantois accord with the results of earlier heterotopic transplantations at headfold stages (Downs and Harmann, 1997), which revealed that distal cells were more restricted in potency than basal ones. Our present findings show that such regional differentiation is established even earlier than previously reported, begin already evident at the late neural plate stage."

Downs, et al., 1998, p. 4515, Fig. 6. This series of brightfield photomicrographs demonstrate spectacular vascularization of allantoises explanted at headfold stages, prior to when they contain obvious blood vessels and prior to fusion with the chorion.

Downs, et al., 2001. The entire paper is devoted to the characteristics of whole allantoises cultured in isolation, prior to when they contain obvious blood vessels and prior to fusion with the chorion, and the effect of various growth conditions on blood vessel formation. Please see especially Figs. 1 and 3.

5. I also wish to comment on the Examiner's statement on page 11, last paragraph, last sentence:

> "The allantoises of Downs [Downs and Gardner, 1995] were labeled with [3H]methyl thymidine (p. 408, column 2, paragraph 3) which is equivalent to applying a test compoundt o a cultured allantoic explant as claimed . . . . The effect of [3H]methyl thymidine on growth and development was observed (page 409, column 1, line 14)."

The whole point of using [3H]thymidine in this context was as a marker to distinguish donor from host allantoises in the grafting experiments designed to discover how chorio-allantoic union occurs. It had nothing to do with allantoic vasculogenesis; "growth and development" refers to growth and development of the entire conceptus, to make sure that tritiated thymidine did not harm the conceptuses. If it did, we would not be able to use it as a marker to distinguish donor allantoic tissue in host conceptuses.

I declare that all statements made herein of my own knowledge.are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the

validity of the above-identified application or any patent issuing thereon.

Respectfully submitted

Date	Karen M. Downs